REMARKS

Upon entry of the amendments, claims 1-15, 17, and 18 constitute the pending claims in the present application. Applicant has amended claims 1-15. Claim 1 was amended to more particularly point out certain aspects of the invention. Claims 2-15 were amended, for example, to provide antecedent basis and multiple dependencies. Claim 16 was cancelled without prejudice. Applicant reserves the right to pursue the subject matter of the cancelled claim in similar or differing scope in this or future applications. New claims 17 and 18 have been added. The claim amendments and new claims are fully supported by the specification. No new matter has been introduced. Applicant respectfully requests reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

Claim Objections

Claims 4-16 were objected to as being in improper form because a multiply dependent claim cannot depend from another multiply dependent claim. Applicant has amended claims 4-15 to correct their form, and have cancelled claim 16. Withdrawal of the claim objection is respectfully requested.

Drawings

The Examiner objected to color drawings. Applicant hereby submits black and white copies of the figures submitted with the instant application. The new figures introduce no new matter. Applicant respectfully requests withdrawal of this objection.

Claim rejections under 35 USC §102(b)

Claims 1-3 were rejected under 35 U.S.C. §102(b) as being anticipated by U.S. Patent Application Publication No. 2001/0044940 (Gorlach *et al.*). The Examiner alleges that Gorlach *et*

al. disclose quantifying mRNA in a sample by using microarrays of DNA probes. Applicant traverses in light of the claim amendments and the following remarks.

Claim 1 recites "a. providing a DNA microarray comprising a plurality of immobilized probes and including one or more dilution series of control spots". Gorlach *et al.* do not teach the use of a dilution series of control spots. Therefore, Gorlach *et al.* do not teach all features of claim 1.

Furthermore, Gorlach *et al.* teach, in paragraph 081, that "Another approach for discovering the function of genes utilizes gene chips and microarrays. DNA sequences representing all the genes in an organism can be placed on miniature solid supports and used as hybridization substrates to quantitate the expression of all the genes represented in a complex mRNA sample." From the specification of Gorlach *et al.*, it is evident that Gorlach *et al.* use microarray analysis for the traditional purpose of **relative** quantification of RNA levels. Claim 1 recites a method of obtaining reference data from a sample and "e. using said reference data to calculate absolute mRNA concentrations in said sample". The control spots, not taught by Gorlach *et al.*, permit the absolute quantity to be determined by providing an internal standard of calibration. Since Gorlach *et al.* do not teach a method of determining **absolute** quantities of mRNA, Gorlach *et al.* cannot anticipate claim 1.

Applicant therefore submits that claims 1-3 are not anticipated by Gorlach *et al.* Reconsideration and withdrawal of this rejection is respectfully requested.

Claim rejections under 35 USC §112, second paragraph

Claims 1-3 are rejected under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Specifically, the Office Action asserts that there is insufficient antecedent basis for the term "the hybridization" in claim 1. Claim 1 has been amended to recite "deriving reference data from step c" rather than "deriving reference data from the hybridization".

The Examiner also asserts that there is insufficient antecedent basis for "the immobilized probes" in claim 2. Claim 1 has been amended to recite "having a plurality of immobilized probes" in order to provide antecedent basis.

Furthermore, the Examiner asserts that there is insufficient antecedent basis for "the array" in claim 2. Claim 2 has been amended to recite "microarray" rather than "array" in order to provide antecedent basis.

The Examiner asserts that claim 1 is confusing as to the metes and bound of "control spots". Applicant respectfully traverses. Applicant asserts that the term "control spots" would be easily understood by one of ordinary skill in the art based on claim 1, the specification, and the state of the art. In paragraph 12, the instant specification defines a "spot" as "a single location on a microarray where only one species of DNA fragments is bound." The specification further elaborates the concept of the control spot in paragraph 9, describing a "dilution series of control DNAs" present on the microarray. Furthermore, claim 1 step a recites all the limitations necessary to understand the concept of "control spots". Claim 1 step a recites "providing a DNA microarray comprising a plurality of immobilized probes and including one or more dilution series of control spots". Thus, Applicant respectfully submits that claim 1, in combination with the specification and the state of the art, clearly defines the metes and bounds of "control spots."

The Examiner also alleges that claim 1 is indefinite with respect to what the microarray is made of. Applicant asserts that the compositions suitable for manufacturing a microarray are well understood by one of ordinary skill in the art. The instant specification acknowledges the state of the art, stating in paragraph 9 that microarrays are "mostly glass chips with chemically modified surfaces". The specification further describes the state of the art in paragraph 2, stating that "representative single stranded DNA fragments are immobilized on a solid support (e.g. a glass slide) to probe for complementary cDNAs or cRNAs." In light of the substantial knowledge available to the skilled artisan in the art, Applicant respectfully asserts that claim 1 is not indefinite.

On page 4 of the Office Action, the Examiner alleges that claims 1-3 are incomplete because they fail to "set forth how the microarray is 'used' in accordance with step e." Claim 1 as amended

now specifies that one may use the microarray by "b. hybridizing the immobilized probes [of the microarray] with the sample or cDNA made from the sample" and "hybridizing the immobilized probes with a corresponding control DNA of known concentration".

The Examiner states that claim 3 is confusing as to recitation of "a DNA microarray." Applicant has amended claim 3 to recite "the DNA microarray". Applicant believes that this amendment eliminates any confusion regarding claim 3.

In light of the claim amendments and remarks above, reconsideration and withdrawal of this rejection is respectfully requested.

Claim rejections under 35 USC §101

Claims 1-3 are rejected as allegedly failing to be supported by either a specific, substantial, and credible asserted utility or a well-established utility. Applicant respectfully traverses on the following ground.

Applicant asserts that the specification supports a specific, substantial, and credible utility. Claim 1 recites a "method for determining the absolute quantity of one or more mRNA molecules in a sample". It is well known in the art that it is useful to determine the absolute concentration of one or more mRNAs. For example, researchers frequently use quantitative PCR on a cDNA sample, using DNA standards of known concentration, to determine the absolute concentration of mRNA. Researchers also use RNase protection assays, with a control RNA of known concentration, to determine the absolute quantity of mRNA. Accordingly, a new method for determining the absolute concentration of mRNA would be equally useful.

Applicant further asserts that the specification indicates at least one specific use for the claimed method. For instance, Table 3 illustrates that the exemplified microarray included spots corresponding to several known yeast genes. Thus, the claimed method may be used to measure the abundance of known yeast transcripts. MPEP 2107 II.A3 states: "If at any time during the

examination, it becomes readily apparent that the claimed invention has a well-established utility, do not impose a rejection based on lack of utility." Since Applicant has shown that the claimed method may be used, for example, for quantifying levels of known yeast transcripts, the claimed methods have utility and comply with 35 U.S.C. 101.

Based on the specification and the state of the art, it would be clear to one skilled in the art that for any method using traditional microarrays for relative quantification of mRNA, one may substitute the claimed method to achieve absolute quantification of mRNA. The utility of traditional microarrays is well known in the art. For instance, microarrays are known in the art to be useful for measuring levels of useful RNAs including endogenous transcripts, exogenous transcripts, *in vitro* transcribed RNA, and *in vitro* synthesized RNA. (See, for example, Zhang *et al.* "Large-scale gene expression data analysis: a new challenge to computational biologists." Genome Res. 1999 Aug;9(8):681-8, and Gray *et al.*, "Genome changes and gene expression in human solid tumors." Carcinogenesis. 2000 Mar;21(3):443-52. Copies of these documents are provided as Exhibits A and B.) In fact, Zhang *et al.* specifically point out the utility of microarrays by writing on page 681, "[t]he use of high-density DNA arrays to monitor gene expression at a genome-wide scale constitutes a fundamental advance in biology." The specification distinctly points out the advantages of the claimed method relative to traditional microarrays. For instance, the specification states in paragraph 3 that "[t]he technique of "spotted" cDNA chips has found widespread use, but allows currently to measure only relative changes of mRNA concentration in a cell." The specification further states in paragraph 5 that "[t]he object underlying the present invention is to provide an improved method and system for determining absolute mRNA quantities" and in paragraph 6 that "[t]his object is achieved with the subject-matter as recited in the claims." Thus, methods of using traditional microarrays have well-established utility and the claimed methods have clearly articulated advantages to traditional methods. Accordingly, the specification instructs one of ordinary skill in the art how to use the claimed methods.

Claim rejections under 35 USC §112, first paragraph

Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph. Specifically, the examiner alleges that the claimed invention is not supported by either a specific, substantial, and credible asserted utility or a well established utility for the reasons set forth above. The examiner further asserts that one skilled in the art would not know how to use the claimed invention. Applicant traverses for the same reasons presented in the above response to the rejection under 35 U.S.C. 101.

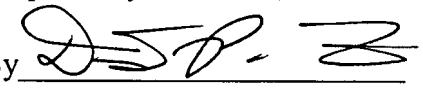
Conclusion

In view of the above amendments and remarks, Applicant believes the pending application is in condition for allowance.

Enclosed is a three month petition for extension of time and payment of the prescribed fee. Payment of the additional claims fee is also provided. Applicant believes no further fees are due with this response. However, if a fee is due, please charge our Deposit Account No. 18-1945, under Order No. VOSS-P01-011 from which the undersigned is authorized to draw.

Dated: November 16, 2007

Respectfully submitted,

By 

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